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09/122,427	07/24/1998	YIYU ZOU	UTSC584USC2	4389

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT

PAPER NUMBER

1615

DATE MAILED: 07/12/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/122,427

Applicant(s)

Zou

Examiner

Gollamudi Kishore

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on May 1, 2002
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1, 3-9, and 52-81 is/are pending in the application.
- 4a) Of the above, claim(s) 57-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3-9, 52-56, and 66-81 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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### **DETAILED ACTION**

**The declaration, the request for the extension of time and amendment filed on 5-1-02 are acknowledged.**

- 1. Newly submitted claims 57-65 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: these claims are drawn to a product produced by a specific process and the product claimed clearly sets forth that the solution at the time of lyophilization does not contain liposomes (meaning that the lyophilate does not contain liposomes) whereas the lyophilate in claim 1 need not be liposome free . The claims have different scope.**

**Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 57-65 have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.**

**Claims included in the prosecution are 1, 3-9, 52-56 and 66-81.**

### ***Claim Rejections - 35 USC § 112***

- 2. The following is a quotation of the second paragraph of 35 U.S.C. 112:**

**The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

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3. Claims 1, 3-9 and 66-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants amend claim 1 recite 'preliposome-lyophilate comprising a non-lipid surfactant. Does this mean that the lyophilate contains only the surfactant, but no lipid? If so, it is unclear how lyophilates containing only Tweens recited in the dependent claims as the surfactant can form liposomes.

Claim 66 is confusing; which one is 'about 4 mole % or less'? The surfactant or the lipid?

*Claim Rejections - 35 U.S.C. § 102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 66-67, 72-73 and 75 are rejected under 35 U.S.C. 102(b) as being anticipated by Mehta (4,950,432).

Mehta discloses preliposomal powders containing a drug and a mixture of phospholipids (note the abstract, columns 6-7, Examples and claims). This rejection is made on the basis of the confusing language of the claim as indicated above in the 112, second paragraph rejection. '4 mole % or less' recited in the independent claim 66 can be

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**interpreted as that pertaining to the surfactant and the term, 'less' includes zero amounts.**

**In other words, the surfactant need not be present at al.**

**(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.**

- 6. Claims 66-67 and 72 are rejected under 35 U.S.C. 102(e) as being anticipated by Mehta (5,811,119).**

**Mehta discloses preliposomal powders containing retinoic acid and a mixture of phospholipids (note the abstract, columns 6-7 and Examples). As pointed out above, these claims could be interpreted as having no requirement for the surfactant and hence the rejection.**

**Applicant's arguments with regard to the previous 102 rejections have been considered, but are deemed to be moot since those claims have not been included in the rejections.**

***Claim Rejections - 35 U.S.C. § 103***

- 7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:**

**(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the**

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prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1, 3-9, 52-56 and 66-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta (4,950,432) or (5,811,119) cited above, further in view of Unger (5,585,112), Isliker (5,089,602), Hsu (5,653,996) individually or in combination.

The teachings of Mehta (432) and (119) have been discussed above.

Mehta in these patents does not disclose the use of surfactants such as Tweens in the preliposomal preparations.

Unger teaches that non-ionic detergents such as Tweens stabilize the liposome compositions (note col. 25, lines 38-48).

Isliker similarly teaches that Tweens could be used in liposome preparations; the liposome preparations are then lyophilized (Example 11).

Hsu teaches the use of Tweens in liposomal preparations (note col. 5, line 25 et seq.).

In essence, the secondary references all teach the routine practice in the art of the use of Tweens in liposomal preparations. Unger in particular teaches that these are liposomal stabilizers. The use of Tweens in the preparations of Mehta would have been obvious to one of ordinary skill in the art since these are stabilizers and routinely used in the art in liposomal preparations.

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**Applicants' arguments have been fully considered, but are not found to be persuasive. Applicants' arguments with regard to Mehta pertain to the 102 rejections; the argument provided applicant with regard to the 103 rejection is that Mehta does not teach Tweens. In response, the examiner points out that the secondary references teach Tweens in liposomes. Applicant further argues that Mehta does not teach the advantage of fast and convenient reconstitution of liposomes having relatively small diameter upon the addition of an aqueous solution. This argument is not found to be persuasive since Mehta's method of preparation also results in the formation of liposomes of by the incubation of the powder with an aqueous medium for 1 to 10 minutes and applicant has not shown that the diameters of liposomes in Mehta are different.**

**Applicant argues that Unger teaches gas filled liposomes and such liposomes are extremely large whereas in instant application the liposomes are less than 400 nanometers and that this size disparity alone teaches away from combining Unger. This argument is not found to be persuasive since Unger's statements col. 25, line 38-48 reflect that Tweens are added to increase the stability of the liposomes which are formed and taken together with Unger's statements on col. 26, lines 31-61 that the sizes of the liposomes will depend upon the intended use and that the preferred lower range is 30 nm, one of ordinary skill in the art would be motivated to include Tweens in Mehta's preliposomal powders since the liposomes formed by hydration of the powders would be expected to have stability because of the presence of Tween.**

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**Applicants' arguments that Isliker discloses a process for the manufacture of apolipoproteins and the disclosure of Isliker is therefore not even directed to a liposomal preparation, but to apolipoprotein preparation are not found to be persuasive since Example 11 of Isliker clearly indicates the preparation of liposomes containing apolipoproteins and not just apolipoproteins and instant claim language does not exclude the presence of apolipoproteins.**

**Applicants' arguments with regard to Hsu are not found to be persuasive. Applicants' arguments essentially are directed to the method of preparation of liposomes; these arguments are not found to be persuasive since irrespective of the method of preparation, Hsu essentially teaches the addition of Tweens in the liposomal preparations and as applicants themselves recognize, Hsu also teaches the lyophilization of the liposomes to prepare powders. With regard to applicants' arguments that Hsu's liposomes contain lung surfactant protein, the examiner points out that instant claims do not exclude this protein.**

**In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only**



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from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The declaration of Roman Perez-Soler submitted by applicants has been carefully reviewed, but is not found to be persuasive since the declaration is not based on Dr. Perez-Soler's interpretation of the prior art used in the rejection and not based on any experimental comparison.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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**10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.**

**The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.**

**If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.**

**Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].**

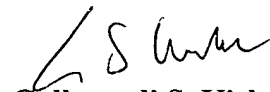
**All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.**

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**Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.**



**Gollamudi S. Kishore, Ph. D**

**Primary Examiner**

**Group 1600**

*gsk*

**July 12, 2002**